Faculty and PostDoc
Population, Health & Wellness

Effect of Omega-3 Polyunsaturated Fatty Acids on Inflammatory Biomarkers in Chronic Obstructive Pulmonary Disease

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ABSTRACT

Chronic obstructive pulmonary disease (COPD) is a chronic progressive inflammatory disease characterized by airflow limitation. Several pro-inflammatory markers are thought to be involved in the pathogenesis of COPD. Cigarette smoking is a major risk factor for COPD, and diet may be a modifiable risk factor for its progression & management. Dietary supplementation with omega-3 polyunsaturated fatty acids (omega-3 PUFAs) may be effective therapeutically in patient COPD. Aim: To determine the plasma basal level of inflammatory biomarkers in the study population, to determine the inflammatory biomarkers release from Peripheral blood mononuclear (PBMCs), and to investigate the effect of omega-3 PUFAs, on inflammatory biomarkers released from PBMCs. Methods: Blood samples were collected from 42 subjects; patients with COPD, 15 healthy smokers (HS), and 12 healthy groups (HNS). Selected biomarkers level was measured in Plasma and PBMCs by ELISA. Individual lipid profile analysis was carried out on RBCs fraction. Result: Plasma high levels of CRP and Fibrinogen and low level of CC-16 were observed in COPD patients when compared with healthy controls. The basal release of IL6, IL8, TNFα, and CD31 from PBMCs was significantly differing in COPD and HS groups compared to HNS group. Omega-3 PUFA (EPA and DHA) reduce IL-6, IL-8 and TNF-α release from PBMCs. The fatty acid composition of the erythrocyte membranes in patients group was unmodified. Conclusion: This study showed that high level of several biomarkers that were detected systemically in COPD group may associate with the disease systemic inflammation. EPA and DHA possess the ability to reduce the cytokines production from COPD inflammatory immune cells. Additionally, no correlation was observed between fatty acid profile analysis and COPD.

INTRODUCTION

COPD is a multicomponent chronic lung disease that decreases quality of life due to shortness of breath and chronic cough. Alterations in the lungs including, destruction of the lung parenchyma and alveoli, inflammation of the central airways with chronic bronchitis, and inflammation of the small airways with chronic bronchiolitis (Tuder and Petrache, 2012; Caramori *et al.,* 2014). This result in dyspnoea, progressive airflow obstruction that is not fully reversible, productive cough, fatigue, and exacerbations (Fulton et al., 2013). Lung inflammation can pass through the systemic circulation causing systemic inflammations and comorbidities, including cardiovascular disease, lung cancer, skeletal muscle dysfunction, diabetes, osteoporosis, and cachexia. (Lee *et al.,* 2018).

Several biomarkers involved in the pathophysiology and inflammatory process of COPD have been identified and measured, but little is known about their relationship to COPD development, progression and severity (Korani *et al.,* 2016). There is a need for biological biomarkers for better evaluation of patients with COPD. This study aims to test the hypothesis that levels of inflammatory biomarkers are increased in circulation and from inflammatory cells in patients with COPD comparing to healthy subjects. Identification of plasma, pulmonary, and inflammatory immune cell biomarkers may facilitate improved diagnosis and prognosis in COPD.

RESULTS

- Linear regression analysis showed a significant correlation between FEV1% and age (P=0.0009) and BMI (P=0.024) of the entire study subjects (P>0.05), and a significant correlation between FEV1/FVC ratio and age (P<0.0001), BMI (P=0.0009) as well as weight of entire study subjects (P=0.022) (Figure 1).
- The mean value of plasma level of CRP was significantly higher in patients with COPD (4.48±28 mg/l) when compared to those of healthy nonsmoking individuals (2.27±2 mg/l) (p =0.007). Mean value of fibrinogen was significantly higher in COPD patients (409±181mg/dl) when comparing with healthy smokers (136±66 mg/dl) (p <0.0001). The mean value of CC16 was significantly lower in plasma of COPD group (2.75±1.19 ng/ml) compared to healthy nonsmoking group (5.77±2.66 ng/ml) (p =0.014) (Figures 2)
- PBMCs obtained from COPD patients, released greater amounts of IL-6 (4±0.46 ng/ml), IL-8 (16.3±0.22 ng/ml), and TNF-α (219±12 pg/ml), compared to those obtained from healthy nonsmokers (p<0.001) (Figures 3).
- There were no significant differences in fatty acids measurements (ARA/EPA, omega-3 PUFA/total PUFA% and Omega 3 index) between the COPD group, healthy smokers and healthy nonsmokers groups (Figure 4).

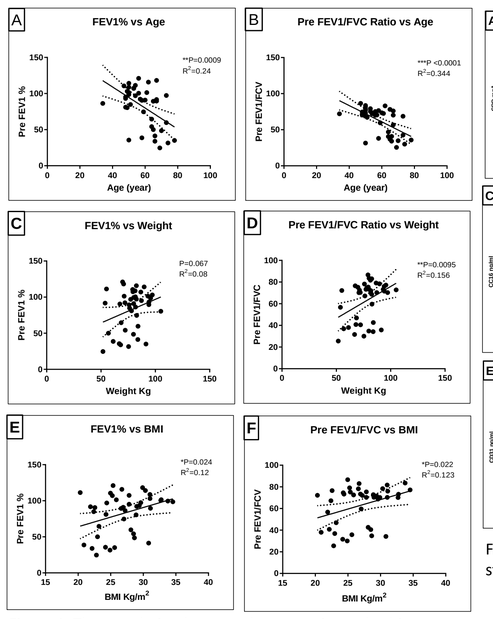


Figure 1. The correlation between lung severity and subject parameters

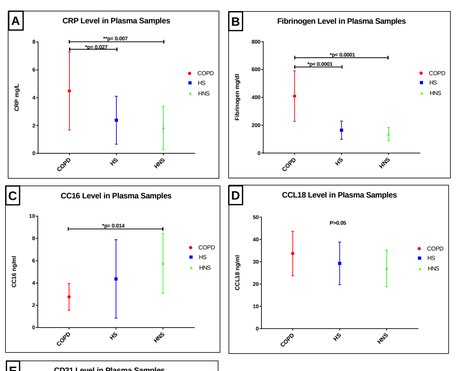


Figure 2. The plasma level of biomarker candidates in the studied groups

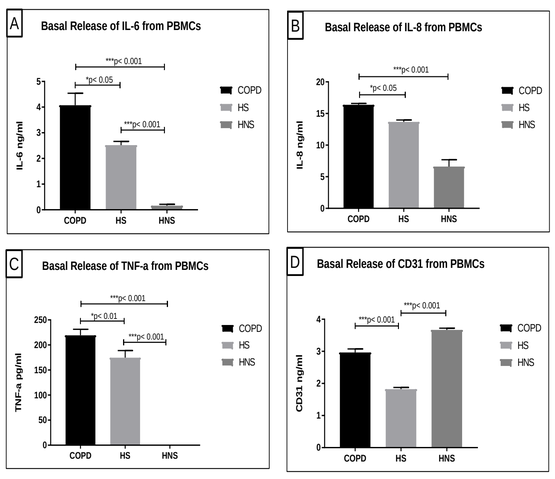


Figure 3. Basal releases of Biomarkers from PBMCs culture samples

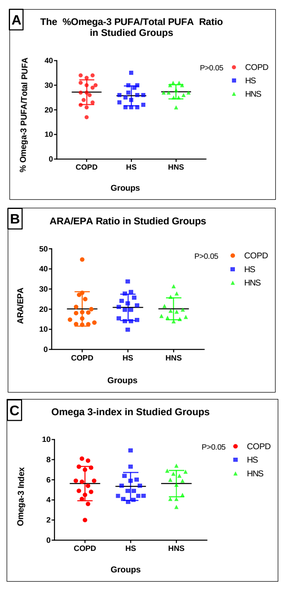
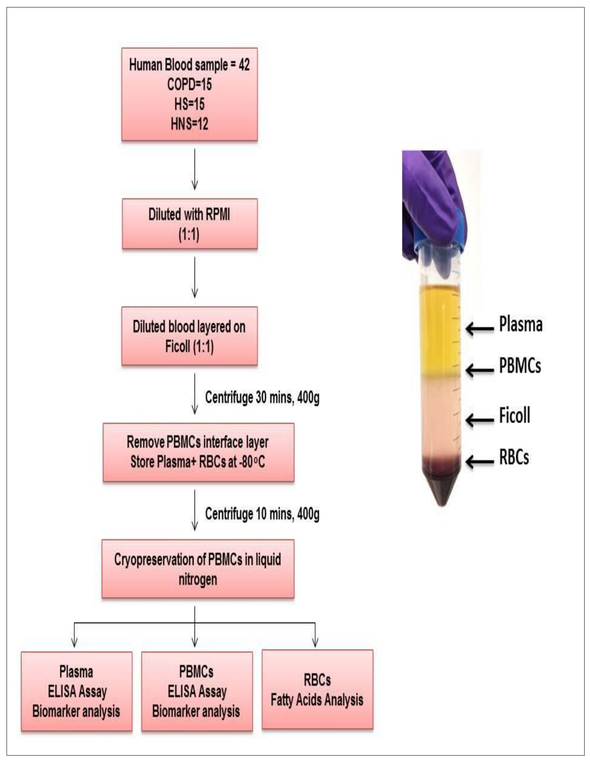


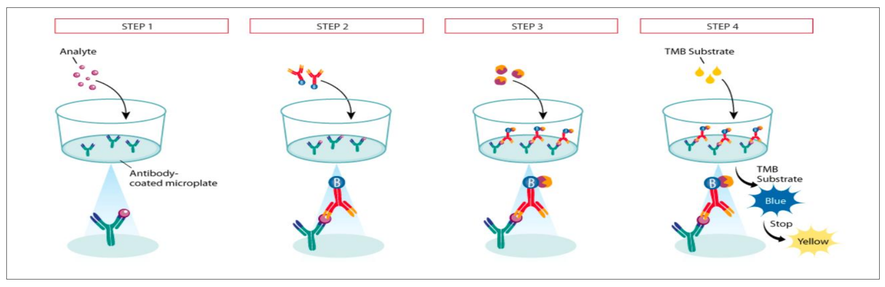
Figure 4. Comparison of (A) omega-3 PUFA/total PUFA, (B) ARA: EPA ratio, (C) omega-3 index.

METHODOLOGY

- Collection and Processing of Blood Samples
- Purification of PBMCs by Ficoll Density Gradient Protocol
- Measuring the level of inflammatory biomarkers in plasma samples
- Biomarker release from unstimulated ex-vivo PBMCs
- Effect of EPA/DHA on Inflammatory Biomarker Production in PBMCs
- Anti-inflammatory actions of EPA and DHA on cytokine release from PBMCs
- Determination of RBC Fatty Acid Profile of Participants



The Ficoll density gradient techniques for separation of PBMCs



DouSet ELISA system Assay principles

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CONCLUSION

Subject parameters; age, weight and BMI, have an impact on subject respiratioty functions when investigatin the whole study indviduals. High level of plasma CRP, fibrinogen, and low level CC16 were associated with COPD, which suggests that CRP, fibrinogen, and CC16 might be a useful biomarker panel related to the presence of COPD. Circulating PBMCs isolated from COPD patients show a profile of pro-inflammatory biomarkers distinct from control PBMCs. The data also confirmed that EPA and DHA individually exerted potential immunomodulatory effects characterized by significant reductions in PHA-induced cytokines release. Additionally, RBC membrane Omega-3 PUFA does not seem to have a major protective effect on lung function or disease symptoms. For better understanding of the COPD variability between patients, different parameters should be evaluated during patient diagnosis at routine clinical practices, including lung plethysmography, gas transfer, arterial oxygen, and CT, Pulmonary and systemic markers, and multiple spirometry. This will provides with accurate diagnosis and better disease management.

ACKNOWLEGEMENTS

This work would not have been possible without the financial support of QATAR University, College of Health Sciences. Also I would like to thanks all my colleagues at work for their support, and cooperation I value a lot. I would like also to express my sincerest gratitude to my supervisor, Dr. Jeremy Allen, who has supported me throughout my thesis with his patience and knowledge. I am extremely grateful to the academic team in Medicines Evaluation Unit (University Hospital South Manchester) for their hard work in collecting the data and providing me with samples. I am grateful to all of technical staff for their help in the lab during the project (University of Salford Manchester).